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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STRZELECKA, TERESA E	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 01/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,543	BYRD ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,13-16,34,35,54,58 and 59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,13-16,34,35,54,58 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This office action is in response to an amendment filed November 4, 2003. Claims 1 and 3-57 were previously pending, with claims 7-12, 17-33, 36-53 and 55-57 withdrawn from consideration. Applicants amended claims 1, 6, 13-16, 34, 35 and 54, cancelled claims 7-12, 17-33, 36-53 and 55-57, and added new claims 58 and 59. Claims 1, 3-6, 13-16, 34, 35, 54, 58 and 59 are pending and will be examined.

2. Applicants' amendments overcame the following: objections to claim 4; rejection of claims 34, 35 and 54 under 35 U.S.C. 112, second paragraph; rejection of claim 54 under 35 U.S.C. 102(b) over Perkin Elmer Cetus catalog. All other rejections are maintained for reasons given in the "Response to Arguments" section.

3. This office action is made non-final because of new grounds for rejection.

Response to Arguments

4. Applicant's arguments filed November 4, 2003 have been fully considered but they are not persuasive. Applicants argue that the Lee et al. do not anticipate amended claim 1, which contains a limitation of an isolated nucleic acid comprising, in addition to at least one Ter-binding site, at least one recombination site. However, Applicants did not define what a "recombination site" is, therefore it can be interpreted as any nucleic acid sequence. Therefore, since Lee et al. teach plasmids containing Ter-binding sites, they also teach recombination sequences.

Applicants further argue that Neylon et al. do not anticipate claims 13 and 14, because they do not teach recombination sites. Again, since Applicants did not define what a "recombination site" is, this term can be interpreted as any nucleic acid sequence. Therefore, since Neylon et al. anticipate claims 13 and 14. Applicants argument regarding the rejection of claims 15 and 16 over Neylon et al. and Gold center again on the fact that Neylon et al. do not anticipate claims 13 and 14,

because they do not teach recombination sites. However, since the recombination site can be any sequence, the combination of Neylon et al. and Gold makes claims 15 and 16 obvious.

The rejections are maintained.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 3-6, 13-16, 34, 35, 54, 58 and 59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID NO: 1-25. No sequences were provided for the recombination sites.

Thus, applicant has express possession of only twenty five particular Ter sites, in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences, which meet these functional limitations, is provided.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the Ter-binding sites lack any specific structure, is precisely the situation of naming a type of material which is generally known to likely exist, but, except for the twenty five specific sequences, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to "an isolated nucleic acid molecule comprising at least one binding site for a Ter-binding protein", for example.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a Ter-binding site, without any definition of the particular site claimed.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise Ter-binding sites represented by SEQ ID NO: 1-25. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

7. Claim 58 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 16 recites the limitation "Ter-site" in line 2. There is insufficient antecedent basis for this limitation in the claim. Claims 13 and 15, from which claim 16 depends, contain a limitation “binding site for a Ter-binding protein”.

B) Claim 58 recites the limitation "Ter-sites" in line 2. There is insufficient antecedent basis for this limitation in the claim. Claim 1, from which claim 58 depends, contains a limitation “binding site for a Ter-binding protein”.

C) Claim 58 is indefinite over the recitation of “wherein the at least Ter-sites”. It is not clear how many Ter-sites should be there.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 3-6, 34, 58 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al. (J. Biol. Chem., vol. 267, pp. 8778-8784, 1992) and evidenced by Bussiere et al. (Mol. Microbiol., vol. 31, pp. 1611-1618; cited in the IDS).

Regarding claims 1 and 58, Lee et al. teach an isolated nucleic acid molecule engineered to comprise two Ter-sites (plasmid oriC-terCW.CCW). The nucleic acid comprises an origin of replication. The Ter sites are arranged with respect to the origin of replication in such a way that the sequence between the Ter sites which does not contain the origin of replication is not replicated in cells expressing a replication termination protein (Fig. 1 (c); Fig. 2, 3).

Regarding claim 3, Lee et al. teach TerB sites (Fig. 1 (c)).

Regarding claim 4, Lee et al. teach plasmids (Fig. 1 (c)).

Regarding claim 5, Lee et al. teach a linear molecule comprising the Ter sites capable of being bound by a Ter-binding protein (Fig. 4 (a)).

Regarding claim 6, Lee et al. teach plasmids comprising restriction enzyme recognition sequences (Fig. 1 (c)).

Regarding claim 34, Lee et al. teach composition comprising plasmid oriC-terCW.CCW and Ter-binding protein (page 8778, the last paragraph, continued on page 8779; Fig. 3).

Regarding claims 35 and 59, Lee et al. teach ter-binding protein (TBP) from *E. coli* (page 8779, first full paragraph). Lee et al. do not use the term "Tus" for this protein. Bussiere et al. teach that the ter-binding protein of *E. coli* is Tus (page 1615, fourth paragraph). Therefore, Lee et al. teach Tus protein.

10. Claims 13 and 14 are rejected under 35 U.S.C. 102(a) as being anticipated by Neylon et al. (Biochemistry, vol. 39, pp. 11989-11999, October 2000; cited in the IDS) as evidenced by Jonsson et al. (Biotechniques, vol. 11, pp. 620-627, 1991).

Regarding claims 13 and 14, Neylon et al. teach a solid support (BIACORE chip) comprising oligonucleotides comprising Ter sites (page 11990, second paragraph; Table 2). Neylon et al. do not specifically teach that the solid support is a non-biological material. However, as evidenced by Jonsson et al., the BIACORE chip consists of glass support coated with gold film, therefore the solid support a non-biological material.

11. Claim 54 is rejected under 35 U.S.C. 102(b) as being anticipated by Pace et al. (U.S. Patent No. 5,681,736).

Claim 54 is drawn to a kit comprising a nucleic acid molecule comprising at least one binding site for a Ter-binding protein and further comprising at least one recombination site, the kit further comprising at least one or more other components. Since the kit does not require an isolated nucleic acid molecule, a kit comprising an E. coli cell, which inherently contains a nucleic acid comprising binding sites for a Ter protein and one of other components would anticipate the claim.

Pace et al. teach a kit comprising enteric bacteria and buffers (col. 11, lines 42-55). Enteric bacteria include E. coli (col. 6, line 40).

Therefore, Pace et al. Teach the limitations of claim 54.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neylon et al. and Gold et al. (U.S. Patent No. 6,242,246).

A) Claim 15 is drawn to a solid support of claim 13 wherein the oligonucleotide is capable of forming a stem-loop or hairpin, and claim 16 is drawn to a solid support of claim 15, where a duplex portion of the stem-loop or hairpin comprises a Ter-site.

B) Neylon et al. teaches an assay which includes binding of Tus to double-stranded Ter sites, but also to single stranded DNA and non-specific sequences. Neylon et al. do not teach oligonucleotides capable of forming stem-loop or hairpin or oligonucleotides with the Ter-sites in the duplex portion of the stem-loop or hairpin.

C) Gold et al. teach solid support with stem-loop nucleic acid molecules which can bind target molecules, such as proteins (col. 4, lines 33-36; Fig. 6; col. 14, lines 26-67;

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the hairpin nucleic acids of Gold et al. in the assays of Neylon et al. The motivation to do so would have been that using hairpin nucleic acids allowed detection of binding to single-stranded (loop of the stem-loop or hairpin) and double-stranded (stem of the stem-loop or hairpin) nucleic acids utilizing single nucleic acid molecules.

14. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gary Benzion will move to the new office on January 22, 2004. His new phone number is (571) 272-0782.

JEFFREY FREDMAN
PRIMARY EXAMINER

TS
January 21, 2004